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EARLY HUMAN EMBRYOS AND THE MODE OF THEIR PRESERVATION.

By Franklin P. Mall, *Professor of Anatomy, the Johns Hopkins University.*

Nearly all human embryos which come into the possession of embryologists are of little value for careful study, because they have been preserved carelessly. Of fifty embryos less than six weeks old, which have come into the writer's hands during the last few years, only six have proved to be of value, and these came from three physicians. In nearly all cases the specimen is destroyed by placing the ovum in very dilute alcohol, and in so doing it is handled very roughly. Poor specimens, however, are better than none at all, therefore in all cases the ova should be preserved, even if there be but little hope to obtain a good specimen. *The best and most convenient method of preserving young embryos is to place the unopened ovum, with the least possible handling, in a large quantity of very strong alcohol.* The alcohol of druggists is in no case too strong, and, according to my experience, is as a rule too weak. Often the ovum is wrapped in a towel and then placed in a small quantity of alcohol and water. This is an excellent method to preserve museum specimens, but it practically ruins every embryo for microscopic study. When an ovum is placed in, say four ounces of strong alcohol, the water of the ovum dilutes the alcohol to a proper strength.

Those physicians who have the proper opportunities should place the specimen as soon as possible, and without opening the ovum, in seventy per cent alcohol, *i. e.*, absolute alcohol reduced by volume to seventy per cent. At the end of a day or two the alcohol is to be renewed, and in this solution the specimen may be preserved indefinitely.

A second convenient method is to place a specimen in quite a large quantity of Müller's fluid, to be changed once or twice during the first few days. The embryo is fully hardened in about a month, and then it is washed in water for a day or two, after which it is to be preserved in seventy per cent alcohol.

Ten per cent nitric acid is a convenient and a most excellent method. The ovum is to be placed in four or six ounces of a ten per cent solution, and opened while in the fluid, care being taken not to injure the embryo. According to its size (if not over an inch long), it should remain in the acid for from thirty minutes to two hours. At the end of this time it is to be placed in seventy per cent alcohol.

Another excellent method is to harden the embryo in saturated aqueous solution of corrosive sublimate. The specimen is to be treated as in the ten per cent nitric acid, but it is to remain in the sublimate longer. These specimens are then to be preserved in seventy per cent alcohol.

There are many other methods, but if any of the above are employed there will be a sufficient supply of material to aid the study of human embryology. It is really wonderful to see what progress has been made in this study when we consider how difficult it is to obtain good material. Some of the most important discoveries have been made in the careful study of a few well-preserved human embryos, as a glance at the many papers of His and the excellent text-book of Minot will show.

Specimens of human ova are not only of value and interest to the embryologist, but are of great importance to the physician in determining the duration of pregnancy. We can easily see why it is easier to determine the age of a young ovum

correctly than to determine the age of the fœtus at full term; in the former the error must be less than a month in order to be overlooked, while in the latter it may exceed this time. Furthermore, in the study of young human ova we may make comparisons with the embryos of other mammals upon which experiment can be made.

Formerly it was quite generally admitted that the age of an embryo is determined by the time of a certain cohabitation. In many cases it was attempted to locate the day exactly. After it had been shown that the ovum is usually extruded from the ovary during menstruation, it was then thought that the egg could be fertilized at any point between the ovary and the uterus. The time required for the ovum to pass through the Fallopian tube was considered the time in which it was capable of being fertilized.

Our most definite information regarding the fertilization of the mammalian ovum has been obtained from experiments upon the dog, rabbit and guinea-pig. In these animals it is found that the spermatozoa pass through the uterus and tubes in from twelve to twenty-four hours after copulation, and await the ovum in the upper part of the tube. The ovum after leaving the ovary enters the tube before it is fertilized by the spermatozoon, and usually begins to divide before it has reached the middle of the tube. After several days the ovum reaches the uterus, and by this time the egg has divided into many cells, which now begin to arrange themselves in layers to form the blastodermic membranes.

It is possible that the spermatozoa retain their power to fertilize for a very long time, if we can judge by their vitality. Piersol* has recently made experiments upon human spermatozoa and finds that they are motile eight or ten days after removal from the body. From this observation it is fair to assume, as he does, that within the uterus and Fallopian tubes their vitality is still greater. However this may be in man, in the lower mammals the arrangement is such that a large number of spermatozoa await the ovum in the upper part of the tube, and furthermore, coitus in rabbits hastens ovulation (Coste).

The evidence from the above observations is that the ova of many mammals are fertilized in the upper part of the Fallopian tube, and there is every reason to believe that the same is true in man. Tubal and abdominal pregnancies speak for this; in the latter form, the placenta is never attached to the peritoneum but to the mucous membrane of the tube, suggesting that the fertilization took place in the beginning of the tube.

Impregnation is nearly always marked by a cessation of menstruation, and it remains to be shown whether or not the fertilization takes place during the last menstrual period or at the time of the first cessation. The experiments upon lower animals show that fertilization of the ovum takes place soon after the rupture of the Graafian vesicle, and it is fair to assume that the same is true in man. After a Graafian vesicle ruptures it is followed by a corpus luteum, but its history is by no means as well known as is generally believed. Our most trustworthy data have been collected by Leopold,† and the more he studied ovaries which had been removed in operations the less definite his conclusions became. We must not lose sight of the fact that the ovaries he removed were to a great extent from women suffering from all kinds of disorders, conditions which no doubt may have complicated his results. In general his conclusion is that a corpus luteum is found in most cases, which from its appearance dates from a menstrual period. During the inter-menstrual period he frequently found in addition to a well-formed corpus luteum, a freshly ruptured follicle, indicating that a second and inter-menstrual ovulation had taken place. This seems to indicate that ovulation takes place more frequently than menstruation. In other cases in which menstrual periods lapsed the women still continued to ovulate. This is by no means remarkable, for it is known that women often become pregnant before menstruation has reappeared during lactation. Also young girls may become pregnant without ever having menstruated.

From all the observations which have been made the conclusion is that in most cases the corpus luteum begins to form some time during menstruation, but it is extremely difficult to locate the exact date. A few of Leopold's cases which are taken from women just before or during the first few days of menstruation are very important regarding this point. In the table the + indicates the probable time of ovulation.

Day of Observation after the beginning of Menstruation.	End of Month.				Beginning of Menstruation.			
	25	26	27	28	Day 1st.	2d.	3d.	4th.
1			+					
2					+			
3				+				
4				+				
26		+						

In these five cases ovulation took place just before menstruation, and we hope that the near future may add a great many more cases to the table, for the removal of ovaries is by no means a rare operation at the present time.

In spite of our ignorance of the relation of ovulation to menstruation, it is quite certain that there must be one, and that when it is better known it will be possible for us to determine much more accurately the age of embryos and the duration of pregnancy than at the present time. The obstetrician is too well aware that an error of several weeks is often made, and really lays no great stress upon the mistake. This error is not very great for a fœtus at full term, but is very serious when the age of an embryo of the first month is to be determined.

The duration of pregnancy has been studied over and over again, and all kinds of views regarding the time of its beginning have been entertained. In nearly all cases the statistics are not complete, and the results are of little value for us to determine accurately the beginning of pregnancy. Hasler*

* Piersol: Anatomischer Anzeiger, 1893.

† Leopold: Archiv für Gynaekologie, Bd. xi u. xxi.

* Hasler: Inaug.-Diss., Zürich, 1876.

in his inaugural dissertation has given us trustworthy data of twenty-eight cases in which the menstrual period, date of cohabitation and the birth of the child are given. In addition he gives an extensive discussion of the whole subject in question. I have tabulated twenty-four of his cases from the twenty-eight, excluding the other four because the data are not complete. In all the cases given the cohabitation did not exceed a day, and it is remarkable that in each case the following menstrual period lapsed. The cases were selected by Hasler with great care and bear every cross-examination. In the table I give the average duration of pregnancy when estimated from the beginning of the last menstruation, in the first column, and when estimated from the day of cohabitation, in the second column.

Time of Copulation.	Number of Cases.	Duration of Pregnancy when estimated from	
		Beginning of last Menstruation.	Day of Copulation.
First week of menstruation.	9	278 days.	273
Second " " "	12	282	272
Third " " "	0	No cases.	No cases.
Fourth " " "	3	299	269

The above table contains our most trustworthy cases, and is of much value regarding the duration of pregnancy. Many other cases are scattered through the literature, and at some future date I hope to tabulate most of them.

Leuckart* has given us data of 110 women, each of whom gave birth to a child within ten months after marriage. The cases were all taken from a single village, and for this reason most of the cases must be trustworthy. In these cases the first cohabitation and the date of the birth of the child are given, but unfortunately the date of the last menstruation is omitted. When the births are tabulated from the date of marriage it is remarkable that the greatest number fall in the 40th and 42d weeks. Stated more accurately, the greatest number fall on the 276th and the 295th days after marriage.

Leuckart believed that these two maxima in the number of births represented the last ovulation before, and the first ovulation after marriage. The 276 days would then represent about 286 days, and the 295 about 285 days.

If we take the three sets of experiments by Leopold, Hasler and Leuckhart we can make them harmonize if we admit that ovulation can take place at any time; it seems as a rule to take place during and immediately after menstruation, and often just before the period. Considering the Graafian vesicle, which is gradually becoming larger and larger, it is fair to assume that its thin wall which is to be ruptured by the hyperæmia of menstruation, can also be ruptured by undue excitement during the inter-menstrual period. This is suggested to us in Hasler's cases in which there was but a single cohabitation in unmarried women. The idea is strengthened by Leopold's study of the corpus luteum, and by the fact that coitus hastens ovulation in lower animals.

From the above statement it is quite evident that our information regarding the rupture of the Graafian vesicle, its relation to menstruation and to fertilization of the ovum, needs a most thorough revision. This cannot possibly be done by one individual alone, and I therefore ask the coöperation of physicians. Each can contribute his part.

Up to the present date our most valuable information regarding the probable time of the fertilization of the ovum has been obtained from the study of a few young human embryos. An error of a few days or weeks would hardly be noticed in a fœtus at full term, but in an embryo two weeks old the same error becomes a matter of great importance. This error has induced embryologists to study the statistics of the obstetricians most carefully.

In order to locate the ovulation from which to compute the age of an embryo, I have tabulated all the young embryos which have been published with a full history. Numbers 2, 3, 4, 6 and 7 are not as complete as they might be, but they are of great value because they fill important gaps. In No. 2 the time between the last menstrual period and the abortion is given roughly as five weeks. Still it is fair to assume that the time must have been between 30 and 40 days. In Nos. 3 and 4 the size of the embryo is not given, but in both cases the ovum is so small that the embryos could not have been over two millimeters long.

From a comparative standpoint we can easily determine the age of human embryos within four weeks. Counting from the last menstrual period, it is quite easy to see by the size of the embryo whether or not it is, say three or seven weeks old. The table shows that, by counting in this way, embryos of the same size may differ four weeks in age (see Nos. 6, 14, 16 and 17). In these cases the ages correspond to those of the other cases, if from their time twenty-eight days are subtracted. This seems to indicate that, as a rule, fertilization of the ovum takes place during the ovulation which precedes the first menstruation which has lapsed. After Reichert had shown that menstruation is only a method of clearing out the uterus after an ovulation, and after Leopold had shown that the mucous membrane of the uterus undergoes histological changes before ovulation, it is fair to assume that the latter changes are only preparatory to the reception of the ovum, and that when the unfertilized ovum reaches the uterus, menstruation is only a method of reducing the uterus to its former condition.

It is necessary to compute the age of the embryo from the last menstrual period in only eight of the cases, and it is not probable that just these eight embryos have grown too rapidly. All the rest must have twenty-eight days subtracted from the time in order to make them correspond with the above eight. These are the main reasons for assuming that the fertilization of the egg takes place just before the first menstrual period which lapsed. It may be that a great many fertilizations take place during the last menstrual period, but that when menstruation has once begun, the activity of the uterus destroys the ovum, and that, as a rule, only those are

* Leuckart: Wagner's Handwörterbuch der Physiologie, Bd. 4.

TABLE OF YOUNG EMBRYOS.

Number.	Observer.	Length of embryo in millimetres.	Beginning of last period.	Last possible cohabitation.	Time of first lapsed period.	Day of abortion.	Time between abortion and: Last period.	Time between abortion and: First lapsed period.	Probable age of embryo.	Number.
1	Mall	.8	January 25.		February 22.	March 7.	41 days.	13 days.	13 days.	1
2	Graf Spee	1.54					5 weeks.	(?)	7 " (?)	2
3	Reichert		October 10.	Early November.	November 7.	November 21.	42 days.	14 "	14 "	3
4	Breuss		×		× + 28.	× + 38.	38 "	10 "	10 "	4
5	Thomson	2.1	×		× + 28.	× + 42.	42 "	14 "	14 "	5*
5*	Mall	2.1	November 7.		December 5.	December 18.	41 "	13 "	13 "	5
6	Thomson	2.5	May 19. (?)			June 1.	14 "		14 "	6
7	His (S. R.)	2.2	August 15. (?)		End of September.	October 14–15.	60 " (?)	14 " (?)	14 "	7
8	His (Lg.)	2.15	September 10.		October 8.	October 20.	40 "	12 "	12 "	8
9	Graf Spee	2.69	×		× + 28.	× + 42.	42 "	14 "	14 " (?)	9
10	Janôsik	3.0	June 1.		June 28.	July 13.	43 "	15 "	15 "	10
11	His (BB.)	3.2	March 26.	April 4.*	April 23.	May 13–16.	48 "	20 "	20 "	11
12	Ecker	4.	August 13.		September 10.	September 27.	45 "	17 "	17 "	12
13	Stubenrauch (K)	4.3	April 10.		May 8.	June 1.	52 "	24 "	24 "	13
14	Wagner	4.5	×			× + 30.	20 "		30 "	14
15	His (a)	4.0	October 4.		November 1.	November 24.	51 "	23 "	23 "	15
16	His (W)	5.0	March 5.			March 26.	21 "		21 "	16
17	Hensen	4.5	×			× + 21.	21 "		21 "	17
18	Stubenrauch (I)	6.0	July 1.	July 8.	July 28.	August 14.	45 "	17 "	17 "	18
19	Stubenrauch (II)	7.0	April 1.	April 14.	April 28.	May 20.	51 "	22 "	22 "	19
20	Mall	7.0	October 6.		November 3.	November 27.	52 "	24 "	24 "	20
21	His (Stt.)	7.75	July 5–8.	July 20.*	August 2–5.	September 1–3.	57 "	29 "	29 "	21
22	Ecker	10.0	April 4.	April 15.	May 2.	June 3.	60 "	32 "	32 "	22
23	His (Br_1)	11.0	April 24.		May 22.	June 24.	61 "	33 "	33 "	23
24	His (Br_2)	13.6	October 20.	End of October.*	November 17.	December 22.	63 "	35 "	35 "	24
25	His (M_3)	13.0	August 7.		September 4.	October 10.	64 "	36 "	36 "	25
26	His (Lhs)	17.	May 4.		June 1.	June 24.	51 "		51 "	26
27	Minot	22.	January 26.		February 23.	March 30.	53 "		63 "	27
28	His	22.	February 21.		March 21.	April 18.	56 "		56 "	28
29	Mall	23.	×		× + 28.	× + 77.	77 "	51 "	51 "	29
30	Minot	32.	January 4.		February 1.	March 13.	68 "		68 "	30

* Earliest cohabitation.

1. Mall: Anatomischer Anzeiger, 1893, p. 630.—2. Graf Spee: Verein Schlesw. Holst. Aerzte, Heft 11, Stück 10; His und Braune's Archiv, 1889, p. 159. 3. Reichert: Abhandl. d. Königl. Akad. d. Wissenschaften zu Berlin, 1873, No. 1.—4. Breuss: Wiener med. Wochenschrift, 1877, p. 502.—5. Thomson: Edinburgh Medical and Surgical Journal, 1839, p. 139; and His: A. m. E., I, p. 152.—6. Thomson: Edinburgh Medical and Surgical Journal, 1839, p. 139; and His: A. m. E, I, p. 152.—7. His (S. R.): A. m. E., I, p 140.—8. His (Lg.): A. m. E., II, pp. 7 and 74.—9. Graf Spee: Verein Schlesw. Holst. Aerzte, Heft 11, Stück 8, 1887.—10. Janôsik: Arch. f. mik. Anat., Bd. 30, pp. 560, 561.—11. His (BB): A. m. E., II, pp. 7, 74.—12. Ecker: His u. Braune's Archiv, 1880, p. 403.—13. Stubenrauch: Inaug. Diss., München, 1889.—14. Wagner: Müller's Archiv, 1835, p. 373.—15. His (a): A. m. E., I, p. 100.—16. His (W): A. m. E., II, pp. 7 and 74.—17. Hensen: His u. Braune's Archiv, 1877, p. 1.—18. Stubenrauch: Inaug. Diss., München, 1889.—19. Stubenrauch: Inaug. Diss., München, 1889.—20. Mall: Journal of Morphology, Vol. 5, p. 459. —21. His (Stt.): A. m. E., II, pp. 8 and 74.—22. Ecker: Icon. Physiol. XXVIII, p. 11.—23. His (Br_1); A. m. E., II, pp. 8 and 74.—24. His (Br_2): A. m. E., II, pp. 9 and 74. —25. His (M_3): A. m. E., II, pp. 9 and 74.—26. His (Lhs.): A. m. E., III, p. 238.—27. Minot: Human Embryology, p. 392.—28. His: A. m. E., III, p. 239.—29. Mall: Not published.—30. Minot: Human Embryology, p. 398.—5*. Embryo from Dr. Ellis, of Elkton, Md.

preserved in which menstruation does not follow the last ovulation. At least the embryological evidence indicates that fertilization takes place just before the first lapsed period, and at present embryologists make their specimens correspond to one another by reckoning the ages of most embryos from the last menstrual period minus twenty-eight days.

The table shows, in addition, that in certain pregnancies the first cohabitation followed the last menstrual period. It cannot be that in these cases the ovum of the last period could have been fertilized, for it is quite certain the ovum loses its power of being fertilized shortly after it leaves the Graafian vesicle.

In case No. 11 (B B), the first cohabitation of a newly married woman took place on April 4, say about five days after the last menstrual period; and the woman ceased menstruating at once, probably on account of the fertilization of the ovum which preceded the first lapsed period. If all the cases of newly married women in which there was an early pregnancy were collected it would, no doubt, be shown that in many of the cases the women did not menstruate at all after marriage. All of Hasler's cases of single cohabitation speak for this.

In several of the cases given in the table, the last cohabitation took place several weeks before the cessation of menstruation, showing that the vitality of the spermatozoa within the female organs lasts for at least a few weeks, or that the last cohabitation was accompanied by an ovulation.

Enough specimens of human ova have been studied and compared with those of lower animals to render it very easy to determine the age of the human from comparative standpoint alone. Thus, for instance, the guinea-pig of two weeks is about as large as the rabbit of the same age. These again are about as large as a dog of three weeks, and all three are of the same stage of development as a human embryo of three and one-half weeks. Then the history of some of the animals closely related to man is now quite well known, and from comparative embryology we can conclude with great certainty whether or not a given ovum is three or four weeks old. In addition to this we have the above table, which cannot be improved much by adding or subtracting a few days from the ages of some of the embryos, as the error cannot be over three days. Therefore we believe that in many cases fertilization of the ovum must take place in the neighborhood of, and usually before some menstrual period. We cannot deny, however, that there may be a difference between the relation of the beginning of pregnancy to menstruation, in first cohabitations, and those which follow later on; in the first, ovulation should be irregular, in the second cases, as regular as it is independently of copulation.

In conclusion, I add a brief history and description of a few young human embryos, and I begin with the youngest which has as yet been cut into serial sections for microscopic study. To be sure, many very young human ova have been seen and the outer forms studied, and the best known of these is Reichert's,* a picture of which is seen in every text-book. Even

*Reichert: Abhandl. d. Königl. Akad. d. Wiss., Berlin, 1873.

such a small thing as an unfertilized human ovum has been found in the Fallopian tube,* showing that with industry and patience "a needle may be found in a haystack." I am under obligations to Dr. Kittredge, of Nashua, New Hampshire, for the above-mentioned specimen. It was quite well preserved when it came into my hands, as it had been placed in a large quantity of sixty per cent alcohol several hours after the abortion. Dr. Kittredge most carefully obtained the history for me, which has borne the most rigid cross-examination in every respect.

"The woman from whom the specimen was obtained is 25 years old, menstruates regularly every four weeks, the periods lasting from four to five days. She gave birth to a child September 19, 1892, and had the first recurrence of menstruation December 19. The second period followed on January 25 and was very profuse; it lasted until February 1. The next period should have begun about February 22, but on account of its lapsing the patient concluded that she was pregnant and called at my office a few days later. I did not examine her, but asked her to remain quiet and await developments, as I thought possible that she might be pregnant. On the evening of March 1 she fell and sprained herself, and during the same night had a scanty flow. The flow recurred each day, and on the seventh of March she passed the ovum. It was kept in a cool moist cloth for twenty hours, and when it came into my hands was at once placed in a large quantity of 60 per cent alcohol." †

The ovum is quite large for its age, having a long diameter of 10 mm. and a short diameter of 7 mm. It is covered with villi only around its greatest circumference, having two spots without villi, as was the case with Reichert's ovum. The villi of the chorion are from 0.5 to 0.7 mm. long and are branched.

Upon opening the chorion it was found that the germinal vesicle was situated just opposite the border of the zone of villi. There was much coagulated albumen around it, which I did not remove and therefore could not obtain good camera drawings. The portion of the chorion to which the vesicle was attached was cut out and stained with alum cochineal and cleared in oil, but even after this treatment it was impossible to obtain any clear picture. The specimen was next imbedded in paraffin and cut into sections 10 μ thick. The series proved to be perfect. From the sections a reconstruction was made in wax, and the accompanying figure (Fig. 1) is a sagittal section of it.

The sections and reconstruction show that the embryonic vesicle is attached to the chorion by means of a stem (*Bauchstiel*). The vesicle itself is composed of two layers, between which, at a distance from the stem, there are indications of blood-vessels or a middle embryonic layer. In the immediate neighborhood of the attachment of the vesicle to its stem there is a deep and short invagination of both layers of the vesicle. At first it was somewhat difficult for me to interpret the meaning of the specimen, because there is as yet no decided mark of the embryonic body. The location of the allantois does, however, give us some clue to the future position of the embryo. It is somewhat complicated on account of the yolk cavity extending into the stem, but I do not think this is serious. I think there is but one rational interpretation of the specimen, *i. e.*, it is an apparent inversion of the membranes, as is the case in many of the rodents. The invagination is the

* Hyrtl: Zeit. f. rat. Med., N. F., IV.

† Letter from Dr. Kittredge, April 27, 1893.

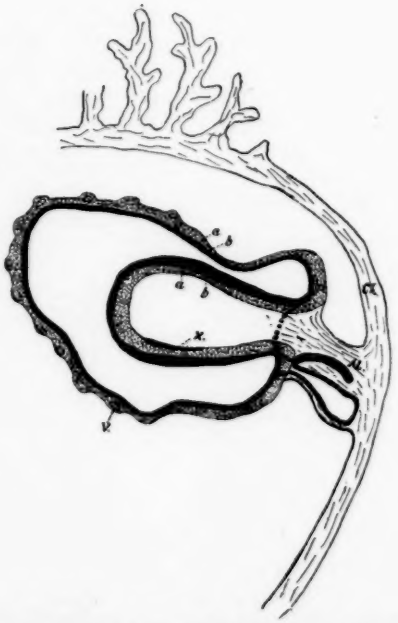

FIG. 1.—Sagittal section of the Kittredge embryo. Taken from the reconstruction. Enlarged 33 times. *Ch*, chorion; *AL*, allantois; *x*, position of embryo; *v*, blood-vessels.

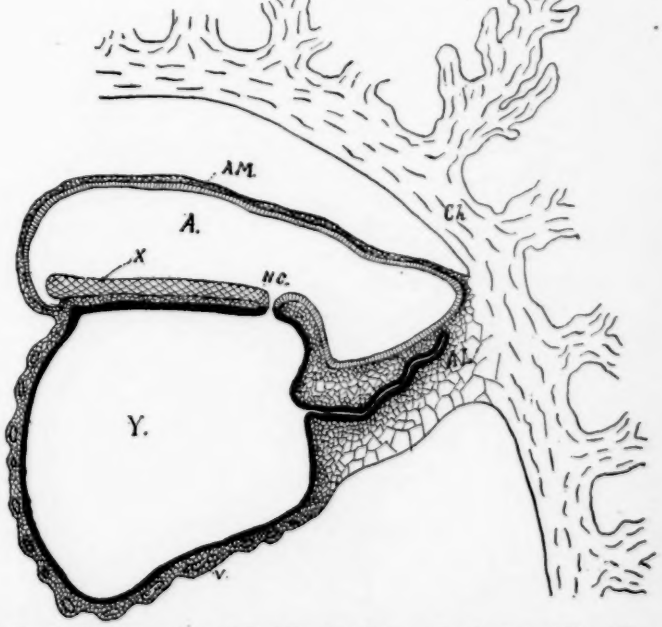

FIG. 2.—Sagittal section of Graf Spee's embryo. *Ch*, chorion; *AM*, amnion; *AL*, allantois; *A*, amniotic cavity; *Y*, yolk cavity or umbilical vesicle; *NC*, neurenteric canal; *X*, embryo: *v*, blood-vessels.

cavity of the amnion. It is comparatively easy for us to imagine how this embryo may be changed into one a little older, as for instance that described by Graf Spee. After the opening of the invagination closes, the walls *a* and *a* approach each other and the layers *b* and *b* move down on either side of the invagination. Then the neurenteric canal breaks through. This is practically the state of things as we find them in Graf Spee's embryo.

The accompanying figure (Fig. 2) is from a sketch by Graf Spee,* which he has kindly permitted me to publish. His original publication† does not give the above picture, which is of such great importance in the study of young embryos, and for this reason I add it. As the figure shows, the yolk-sac occupies nearly the whole length of the embryo, and is not much larger than the amniotic cavity. The embryonic medullary plate, *X*, projects slightly forward to form the head-end of the embryo; it is a broad thickened layer of ectoderm, and seen from above is slightly constricted in its middle. Towards the tail-end of the embryo in the middle line there is a communication between the amniotic and yolk cavities, the neurenteric canal; behind this there is a primitive streak. The neurenteric canal or blastopore is the very interesting part in this embryo, because it is the only instance in human embryology in which this canal has been seen. There are many other parts which have been carefully studied in this specimen, but the few mentioned are sufficient to show the great value of it.

When the sagittal sections of the Spee embryo are placed beside that from Dr. Kittredge, we at once obtain suggestions regarding the early formation of the amnion, allantois and yolk vesicle. These parts are by no means formed in the same way in different animals, and up to the present we have had to content ourselves with a theory by His, which has been extensively copied in the various embryologies.

I have drawn the parts I consider homologous with the same kind of lines. A little imagination, aided by some recent work by Selenka‡ on higher mammals is my reason for believing that the invagination in Fig. 1 is converted into the amniotic cavity of Fig. 2.

After the second week a great number of human embryos have been obtained, many of which have been studied carefully by embryologists, especially Professor His. To give an idea of the growth of the external form of embryos, I add a figure taken from His's Atlas.§ The ages of the embryos selected represent from two weeks up to the beginning of the third month. The embryo from which the smallest figure is taken is slightly larger and older than Graf Spee's embryo, and a week later (3) the form of the body is already outlined. During the fourth week the eye, ear, branchial arches and extremities appear, and in the sixth the leg, foot and toes are quite well formed.

The general conclusions formulated by Professor His to determine the age of human embryos are, when slightly modified, as follows:

* Letter from Graf Spee, April 9, 1893.
† Graf Spee: His u. Braune's Archiv, 1889.
‡ Selenka: Studien, Taf. 41, Fig. 6.
§ His: Anatomie mensch. Embryonen. Leipzig, 1880.

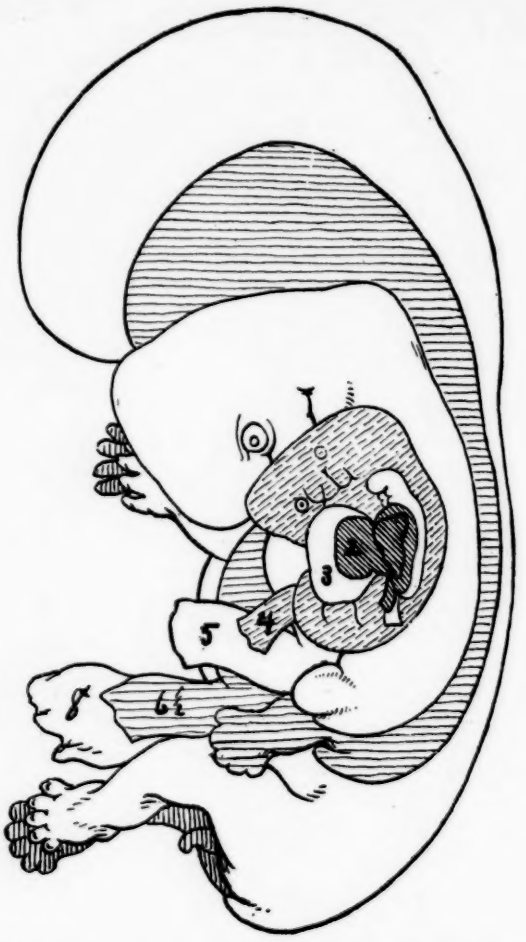

FIG. 3.—Six human embryos taken from His's Standard Chart. Enlarged 5 times. The figures in the cut indicate the age of the embryo in weeks. 2 is His's embryo *SR*; 3, embryo *Lr*; 4, embryo *A*; 5, embryo *C*^{II}; 6½, embryo *XCI*; 8, embryo *Wt*.

1. The beginning of development is the time of impregnation, *i. e.*, at that moment when the spermatozoon enters the ovum.

2. The time the egg leaves the ovary is marked by menstruation, but it is not necessary for the Graafian vesicle to rupture during menstruation; it may take place immediately before, during, or after the hemorrhage.

3. The egg is not capable of being fertilized at any point from the ovary to the uterus, but only shortly after it has left the ovary; as a rule, as it is entering the Fallopian tube.

4. The spermatozoa which have entered the female sexual organs must await the ovum in the upper part of the Fallopian tube, and can retain their vitality here several days, or possibly several weeks. The time of cohabitation is, therefore, not directly related to the age of the embryo.

5. The age of many embryos is to be estimated from the beginning of the first menstrual period which has lapsed,

although it is possible to have a menstruation after fertilization of the ovum.

6. The age of an embryo can be expressed by the following formulas: $A = X - M$ or $A = X - M - 28$, in which X is the date of the abortion and M the beginning of the last period. The second formula is for cases in which it is necessary to count from the first lapsed period.

There is no reason why the gynecologist should not add his share in determining the age af embryos. Any physician can add greatly to the subject if he will record all cases in his practice after the plan of Dr. Kittredge's letter. It is not necessary for him to confine himself to young embryos alone, but he might also include fœtuses at full term; especially those of newly married women will be valuable. Moreover, if the young specimens are carefully preserved, he will do a great work hand in hand with the embryologist.

To facilitate the arrangement of data which may be obtained, I append two tables with a single case in each.

THE HISTORY OF AN EMBRYO.

Beginning of last menstrual period.	Duration of period.	Frequency of periods.	Date of abortion.	Dimensions of embryo.	Remarks.
Oct. 6	4 days	28 days	Nov. 27	Ovum not opened.	Hardened in alcohol 3 hours after abortion.

HISTORY OF A CHILD BORN WITHIN TEN MONTHS AFTER MARRIAGE.

Beginning of last period before marriage.	Duration of period.	Frequency of periods.	Date of marriage.	Dates of periods after marriage.	Duration of last period.	Date of birth of child.	Remarks.
Dec. 10	5 days	28 days	Jan. 1	Jan. 7	days	Oct. 7	Boy, very large.

If there is more than one period after marriage, the date and duration of each should be given.

THE PRESENCE AND ABSENCE OF FREE HYDROCHLORIC ACID IN THE STOMACH.

BY H. SALZER, M. D.

[*Read before the Johns Hopkins Hospital Medical Society, December* 18, 1893.]

By the phloroglucin-vanillin test we are able to detect the faintest trace of hydrochloric acid in the expressed contents of the stomach. The absence of this test, however, does not mean that the stomach does not secrete the acid; the test is only for free acid. The acid, which has become absorbed by albuminoids and in the formation of neutral salts, and is present in the stomach contents, is not shown by the test; still it was secreted and did its work. The search for these compounds is laboratory work, and for the practitioner it is sufficient to know that in the normal healthy stomach at the height of digestion, and in the empty stomach after mechanical irritation, there is free hydrochloric acid, varying in amount from ½ to 2 per mille. All investigations have verified this. We consider the height of digestion an hour after the Ewald test breakfast, or three hours after a more complex dinner.

As regards the quantity of acid present, there are many methods, more or less detailed and cumbersome. Still, by some practice it is not difficult to determine quite accurately and quickly the amount by the Guenzberg test. Some, as Einhorn, prepare different dilutions of the stomach contents and draw conclusions from the intensity of the reaction. I have found that by using a titration method, the modification of the red tint is sufficient to make precise estimates as to quantity. The differences in color acquired by using exactly the same amount of reagent and of hydrochloric acid, diluted to a certain degree, will show you the practical value of this.

In the specimens shown here I have used hydrochloric acid diluted to $\frac{1}{3000}$, $\frac{1}{2000}$, $\frac{1}{500}$, and $\frac{1}{200}$, equal to $\frac{2}{10}$, $\frac{5}{10}$, 2, and 5 per mille; you see the clear differences of the respective proportions. Compared with this, even the simplest methods—as Leo's with carbonate of lime—are of little value to the busy practitioner. I proceed as follows: Put three drops of the Guenzberg reagent and six drops of the stomach contents in a flat porcelain dish—the ordinary butter-plate answers the purpose admirably—and let the reagent and stomach contents mix thoroughly, then place the dish about a foot above a Bunsen flame turned low, and let the mixture evaporate. This takes from ten to fifteen minutes, during which time the attention can be devoted fully to other work.

The fact that the healthy stomach contains free hydrochloric acid would indicate that the absence of acid *per se* expresses pathological conditions. But the diagnostic value of this for cancer and atrophy of the tubules has been considerably modified. According to all authors, in non-compensated heart disease this symptom is quite frequently present.

In my own experience, referring mostly to alterations in digestion, I have found free hydrochloric acid absent in almost one-third of the cases examined. The ease and accuracy of the test exclude every error in this direction. The majority of the patients had comparatively good digestive powers, and the pepsin and rennet functions were more or less normal, but present. Most of them, however, showed an abnormal amount of lactic acid, respectively the corresponding reaction with Uffelman's test. Normally, this reaction is present only in the beginning of digestion, and decreases towards the height of digestion as the hydrochloric acid increases.

The presence of free hydrochloric acid in the empty stomach, without mechanical irritation, is abnormal, as well as an amount of the same exceeding the normal quantity, at the height of digestion, and often reaching from 5 to 7 per mille.

Both these conditions, the hyperchlorhydrie proper, often simply called hyperacidity of the stomach, are frequently observed without any pathological changes, and are then, according to all authorities, considered purely neurotic in origin; of the pathological conditions the peptic ulcer is most frequently met in connection with hyperacidity.

Achlorhydrie—absence of free hydrochloric acid—is frequently to be looked upon as the result of grave circulatory disturbances, especially of those connected with overloading the venous system. This statement, of course, does not comprise cancer and atrophy. It would appear but natural that hyperchlorhydrie, the opposite condition, should be due to the opposite cause, that is, arterial hyperæmia. I have analyzed my cases of this year from this standpoint, as shown in this table. I shall substitute for achlorhydrie, euchlorhydrie, and hyperchlorhydrie, the more common expressions, anacidity, normal acidity, and hyperacidity. It is readily understood that they do not refer to acidity in general, but only to free hydrochloric acid, its absence and its presence in normal or surplus quantities.

TOTAL: 120 PATIENTS; 364 EXPRESSIONS OF STOMACH CONTENTS.

ACHLORHYDRIE: 44 Cases; 139 Examinations.

Essential chronic gastritis	3
Chronic gastritis and dilatation	3
Chronic gastritis, dilatation and atrophy	2
Chronic gastritis, valvular heart disease	3
Chronic gastritis, dilated (fatty) heart	7
Chronic gastritis, cirrhosis of liver	3
Chronic gastritis, parenchym. nephritis	2
Chronic gastritis, interstit. nephritis	1
Chronic gastritis, malaria	1
Chronic gastritis, leukæmia	1
Chronic gastritis, tabes dors	2
Chronic gastritis, gallstones	2
Carcinoma of stomach	1
Carcinoma with atrophy of tubules	3
Leube's nervous dyspepsia	5
Hæmaturia	1
Carcinoma pelvis	1
Carcinoma of kidney	1
Epilepsy	1
Catarrh. antri. Highmor	1

NORMAL CHLORHYDRIE: 33 Cases; 112 Examinations.

Essential chronic gastritis	7
Essential chronic gastritis and dilatation	1
Chronic gastritis, spleen tumor, anæmia	1
Chronic gastritis, valvular heart disease	1
Chronic gastritis, dilated (fatty) heart	1
Chronic gastritis, cirrhosis of liver	1
Chronic gastritis, floating kidney	1
Chronic gastritis, interstitial nephritis	1
Crises gastriques, tabes dorsalis	1
Chronic gastritis, gallstones	2
Nervous dyspepsia, neurasthenia	2
Nervous dyspepsia, hysteria	4
Nervous dyspepsia, floating kidney	3
Peptic ulcer	3
Peptic ulcer, phthisis pulmon	2
Lead poisoning cardialgia	1
Pyelitis	1

ACHLORHYDRIE ALTERNATING WITH CHLORHYDRIE: 18 Cases; 60 Examinations.

Essential chronic gastritis	6
Chronic gastritis, dilatation	3
Chronic gastritis, dilated (fatty) heart	1
Chronic gastritis, parenchym. nephritis	2
Chronic gastritis, interstitial nephritis	1
Nervous dyspepsia, neurasthenia	3
Nervous dyspepsia, hysteria	2

HYPERCHLORHYDRIE: 25 Cases; 53 Examinations.

Chronic gastritis, valvular heart disease	1
Chronic gastritis, dilated (fatty) heart and sciatica	1
Chronic gastritis, interstitial nephritis	3
Nervous dyspepsia, neurasthenia	6
Nervous dyspepsia, hysteria	7
Nervous dyspepsia, floating kidney	1
Peptic ulcer	6

The table comprises only those cases of which I was able to keep records, and enumerates 120 patients with 366 examinations of the stomach contents. While the majority had from two to five examinations, some had as high as 15 and 20. In these 120 cases were 44 cases of anacidity, entire absence of free hydrochloric acid, of which only three were cancer, and only five showed no pepsin or rennet reaction, that is, atrophy of the gastric tubules.

Thirty-nine patients had more or less good digestion despite entire absence of free hydrochloric acid for a long time. Among the patients with valvular disease there is one case of hyperacidity, one with normal acidity, and three with anacidity. Cases with eccentric heart-hypertrophy, resp. dilatation—the majority being probably fatty heart—are comparatively numerous. They are mostly habitual over-eaters with sedentary occupations, and seldom are without dyspeptic symptoms. Of these cases I have one with hyperacidity, one with normal acidity, and seven with anacidity. In perenchymatous nephritis two showed no acid and two normal acidity, while of those with interstitial nephritis with hypertrophy of the left heart I have only one with anacidity and three with hyperacidity.

It is an established fact that nervous dyspepsia and peptic ulcer predispose to hyperacidity. Allow me to remark that a majority of these patients show a nervous heart function. I have nevertheless cases of hysteria and neurasthenia—Leube's nervous dyspepsia—which did not react for hydrochloric acid, and I have one case of dilated heart, impulse not palpable, and one with vitium cordis not compensated, which showed decided hyperacidity. The great majority of the cases, however, seem to sustain the view expressed above, that an overloaded venous system favors absence of free hydrochloric acid, and an arterial hyperæmia tends to produce a surplus of its amount.

I have here the histories of three cases showing absence of free hydrochloric acid for months. This continued even when there was perfect digestion, and the cases showed free acid only after the circulation had been greatly improved. This was accomplished by an entirely changed mode of life. There is also one case of nephritis with no free acid, which after months showed free acid present, at the same time that the left heart began to hypertrophy. Moreover, three cases of

interstitial nephritis with hypertrophy of the left heart showed hyperacidity, despite the absence of any symptom pointing to peptic ulcer. This is very striking, as one would expect just the reverse in such severe lesions. Of course in the latest stages of nephritis this may be different. I have not had an opportunity to investigate this point.

The histories are as follows:

J. W. P., a man, æt. 32, clerk.

January 7.—Patient had been examined two years before and found very dyspeptic. He had slight albuminuria and hyaline casts, and had then complained of being weak, of fullness and pain after eating, bad taste in the mouth, and eructations.

Examination showed the lungs healthy; the heart impulse was weak; the arteries good. Urine showed trace of albumen, sp. gr. 1026; no casts, many urates and indican. A test-meal showed impaired digestion, pepsin and rennet present, but no free hydrochloric acid. The latter was not found, either after test-meals or in the empty stomach, until October—that is, 10 months later. By this time his general condition was much improved, though he complains now a good deal of burning on an empty stomach. There was no albumen in the urine, and no casts were seen. The heart impulse was now comparatively strong. The patient had spent the summer in the country and had led a wholesome life.

C. W. S., a man, æt. 31, traveling agent.

January 13.—The patient had complained for years of depression and dyspepsia, and gave the history of sexual neurasthenia. The examination was entirely negative, except that for three months there was no free hydrochloric acid in the stomach contents. Pepsin and rennet ferment were almost always present in normal proportions. The patient stopped his irregular life and regulated everything—habits, food and exercise. He lived exclusively in the country. His pallid appearance soon gave way to a normal fresh one. Until August—8 months after coming under observation—the stomach showed varying degrees of acidity, from none to hyperacidity. In the last two months the patient has improved, despite temporary nervous spells, and every examination shows free hydrochloric acid.

Mrs. J. R., a woman, æt. 40, a singer.

June 16.—Complained of rheumatic and neuralgic pains at different parts of the body; she was easily fatigued and out of breath.

Examination showed lungs normal; heart was dilated, the first sound quite weak; it was evidently a fatty heart. Urine, sp. gr. 1021, showed indican, a trace of albumen and many urates. Expressed stomach contents after a test-meal showed a low digestion, reacted for pepsin and rennet ferment, though slowly, and showed no free hydrochloric acid. Four weeks later there was still no acid, but the pepsin and rennet reactions were much better, and digestion was normal. Under constant hygienic measures the circulation improved immensely; the symptoms disappeared, and after four months free acid appeared in the stomach contents.

A. H. S., a man, æt. 56, a merchant.

January 12.—Patient had lues when young; of late had much dyspepsia, sick headache and vertigo.

Examination showed lungs and heart normal, arteries sclerotic. Urine, sp. gr. 1007; polyuria—there was ½ to 1 per cent of albumen, and hyaline and granular casts were seen. Repeated stomach examinations showed varying pepsin and rennet reaction, but no free hydrochloric acid. This was in 16 examinations in 8 months. The acid then appeared, and in October and November there was 1 to 3 per mille of acid present. At the same time the heart showed physical signs of commencing hypertrophy of left ventricle.

The urine still shows all the signs of interstitial nephritis.

We consider alterations in the kidney as due to both circulatory and parenchymatous causes and refer them to the primary affection. Now, in the stomach the influence of the locality is quite evident. It is almost certain that the glands of the fundus with the parietal cells (Belegzellen) secrete the muriatic acid; the glands at the pyloric portion appear to have nothing to do with this. The blood-supply of the fundus from the gastro-epiploics is very free, and it is probable that the blood-distribution is an important factor.

There is an analogy between the spastic urination and the hyperacidity of hysterical patients. This urination, as well as that appearing in the chill of malaria, have been thought to be more than neurotic. They are probably also the result of arterial hyperæmia. I think this explanation may also be applied to the hyperacidity in contrast to the lack of acidity being related to venous congestion.

I would refer you to the causal relation chlorosis so frequently bears to peptic ulcer, and to the great increase of the heart's action in the latter disease. Although it is chiefly the right heart that undergoes eccentric dilatation, still there is almost always a strong impulse visible on the left side, pointing to increased action of the left ventricle.

There have been innumerable theories to account for the formation of peptic ulcer. Pavy suggested lack of alkalies in the blood to neutralize the hydrochloric acid; V. Sohlern referred to the want of potash salts. Shiff and Ebstein have shown that incision into the anterior corpora quadrigemina is followed by necrotic processes. Other theories are that of proliferation of cells (Virchow), degeneration of arteries, resulting at times in miliary aneurisms (Welch), capillary hemorrhagic infarcts, trauma, too hot and too cold ingesta, chemical and mechanical irritation, as too coarse food or foreign bodies. Bacterial invasion has been pointed out by Klebs, Boettcher and others. It has been shown that no one of these causes acts alone to produce the ulcer; they merely lower the *vis resistentiæ* of the part, which is then eroded by the hydrochloric acid; and in an exhaustive search of the literature of the subject I have not found any allusion to the difference in venous and arterial pressure—although Ewald refers to the rare combination of peptic ulcer and hepatic cirrhosis, despite the intense hyperæmia (he does not say venous hyperæmia)—yet it seems to me this difference in pressure must be of great importance. I would call your attention to the well-known fact that when the lungs are laden with venous blood there is a great tendency to cirrhosis, chronic inflammation, œdema, etc., but very little tendency to phthisis. This last-named is a comparatively rare complication of valvular heart disease.

Indeed, an experienced practitioner will make a diagnosis of a burst, dilated vein, from the dark venous blood coughed or spit up by a cirrhotic potator; on the other hand, a stream of bright red blood points to phthisis in hæmoptosis, and to peptic ulcer in hæmatemesis.

I am well aware that the difference between active and passive congestion does not depend solely upon an increased or decreased action of the left ventricle, but on the condition of the entire circulatory apparatus, and that for instance we may have hyperacidity despite a weak left heart, though most probably it is even here due to arterial hyperæmia caused by nervous influences.

In general, I believe that the fact that there is absence or decrease of acidity in venous congestion, and hyperacidity in arterial hyperæmia, is well enough established to be of diagnostic and even therapeutic value. For instance, in cases where complete anæmia (as cancer and atrophy) is excluded, we should think of venous congestion and an overloaded right heart as a possible cause of decreased acidity, and similarly in hyperacidity we should look for an over-active left ventricle. In the absence of acid, stimulation of the circulation is indicated, while in hyperacidity we should give sedatives. The success of the strict rest treatment in peptic ulcer seems to me to favor this view.

Of course there are cases of hyperacidity where outdoor exercise is advisable, and again cases of subacidity which require rest. It is well known that a non-compensating and overworked heart needs rest and not exercise, but even here the rest may be looked upon as a stimulus for the weak heart.

Finally, I wish to repeat that decrease and absence of acidity is often identical with venous and hyperacidity with arterial hyperæmia. This, and more especially the unexpected frequency of the absence of free hydrochloric acid in the stomach, are the object of this paper.

IMPORTANCE TO THE SURGEON OF A BACTERIOLOGICAL TRAINING.

By Hunter Robb, M. D., *Associate in Gynecology.*

[*Abstract of an article read before the Clinical Society of Baltimore, December* 1, 1893.]

Among the brilliant results to be obtained from the study of bacteriology, none seems to us of greater importance than the establishment on a scientific basis of a thorough technique in surgical operations.

It will obviously be impossible for a surgeon to have any fixed rules by which he may be guided, unless he has first obtained a true conception of the meaning of the terms *sepsis*, *asepsis*, and *antisepsis*, and is determined at all costs to apply his knowledge to his every-day work. Once again in this connection do we find the old proverb verified, that "experience cannot be bought," for although perhaps the majority of the operators of to-day may theoretically appreciate the dangers of wound infection, and have read or heard of the various means that are to be taken to prevent it, there are comparatively but few who have learned their lesson so thoroughly as to be consistent in the technique which they employ.

It is by no means unusual to hear a surgeon remark that he has performed an "aseptic" operation, or that he always operates "under strictly aseptic precautions," when his technique, as actually observed by one trained in bacteriology, will be found to be woefully defective.

The practical scientific application of an aseptic and antiseptic technique can be thoroughly carried out only by observing every, even the most minute detail, the utility of which has been proved by bacteriological experiment; and although the surgeon who makes use of methods which have been submitted to the tests of bacteriological criticism may attain to a perfected technique, he can never feel so thoroughly at home, or be so appreciative of every step, unless he himself has, by a training in a bacteriological laboratory, obtained exalted ideas of surgical cleanliness, which otherwise he might always feel to be slightly exaggerated. Such a training will open his eyes and enable him to see the many inconsistencies which, trifling as they may appear to the ordinary observer, are too often responsible for the introduction of infectious material into the wound. One would think that an operator, after taking every precaution to render his own hands sterile, would avoid bringing them in contact subsequently with objects which have not been previously sterilized, and yet it is by no means uncommon to see those who are regarded as "careful men" touching with their hands the face or hair, or permitting their hands to come in contact with non-sterile articles, such for example as a blanket which protects the patient, just prior to or during an operation, and proceeding with their work without thoroughly cleansing the hands again.

I remember seeing a surgeon leave the operating table while performing an abdominal section, to pick up an unsterilized instrument which he wished to bend at a certain angle and employ in order to better expose the parts. In doing this he used as a support a table and a chair that happened to be near at hand but which were unsterilized. After having bent the instrument to the desired shape, the surgeon proceeded to employ it immediately without making any attempt to sterilize either it or his own hands. I have seen an assistant, after drawing a ligature between his teeth, thread the needle with it for the surgeon to use in the abdominal wound. Unfortunately, I could multiply such glaring instances of faulty technique, which I should not mention were it not for the fact that errors equally as bad have been observed in men who are considered leaders and to whose lot it falls to instruct others in surgery. While the surgical judgment and skill of such may be undoubted, the technique which they employ is dangerous and pernicious. I do not doubt but that they are thoroughly conversant with the conditions which underlie suppuration in wounds and septic processes generally, and know only

too well how many are the loopholes for infection; but as we all are the creatures of habit, the attainment of a perfected technique will be impossible unless we have schooled ourselves to provide against the unforeseen dangers which are constantly turning up in the operating room. Such a discipline can only be obtained by a thorough preliminary training in a bacteriological laboratory.

It is not improbable, especially in conditions of lowered resistance where the cells and tissue-fluids of the body do not exercise their normal germicidal power, or do so only in a feeble way, that infection may occur even though all possible precautions have been taken by the surgeon and his assistants. Experiments have shown that no method has yet been discovered by which the skin can be rendered absolutely sterile, and that the cutaneous glands contain, even after the most careful disinfection of the surface, micro-organisms which in a proper "soil" are capable of giving rise to inflammation and suppuration. Though it may be true, as has been contended by good men, that every wound made by the surgeon contains micro-organisms, we may assume that under ordinary circumstances the resisting powers of the patient will be sufficient to prevent their growth and development. Experience, however, has taught us that there are several kinds of bacteria which under certain circumstances possess sufficient virulence, that when introduced into the tissues even of a perfectly healthy individual they are capable of setting up violent local or general infections, and what we wish to urge is that every surgeon shall do everything in his power to prevent the ingress of such bacteria. While admitting that infection following an operation must, with our present knowledge, be sometimes attributed to a lowered systemic resistance, and to no fault of the operator or his assistants, it must be insisted upon that this is a very rare occurrence, and that in nearly every case in which suppuration has taken place a rigid analysis of the technique employed will bring to light some sin of omission or of commission to account for it. We believe that a perfected technique can ultimately be attained by submitting every step to the test of bacteriological examination, and the surgeon who works on these lines will *cæteris paribus* undoubtedly obtain the best results, at least in the long run.

That some surgeons do not seem to pay much attention to a careful technique and yet obtain good results is no argument at all against the carrying out of thoroughly scientific procedures. As a matter of fact, a careful investigation of their results and those of their followers, compared with those of aseptic surgeons and their students, will, if a sufficient number of parallel cases be taken, certainly show the inferiority of the older methods.

The term *sepsis* or *septic infection* includes nearly all of the lesions, general or local, resulting from bacterial invasion. The symptoms are due, as a rule, not so much to the direct effect of the bacteria themselves, as to the action of their chemical products. With or without extensive multiplication of the micro-organisms in the blood, the system may be overwhelmed with the bacterial poisons. This condition is called *acute septicæmia.* Localization of pyogenic bacteria in the organs, especially when the bacteria are transported by infectious emboli, gives rise to multiple abscess formation. This condition is called *pyæmia.* Infections partaking of both of these two conditions must be classed as cases of *septico-pyæmia.*

Under the head of *local infections* we at the present day group together all those so-called "accidents" which befall wounds: suppuration, traumatic fever, hospital gangrene, wound diphtheria and erysipelas. All of these, though occurring much more rarely than of old, are still occasionally seen.

General septicæmia or pyæmia may be set up by almost any of the micro-organisms which have pyogenic properties, *i. e.*, which are capable of giving rise to local suppuration. The organisms most frequently met with in surgical experience are: the *staphylococcus pyogenes aureus*, the *streptococcus pyogenes*, and the *bacterium coli commune.* Less frequently we have to deal with the *staphylococcus epidermidis albus*, the *staphylococcus pyogenes albus*, the *staphylococcus pyogenes citreus*, the *gonococcus of Neisser*, the *bacillus of green pus* (bacillus pyocyaneus), the *micrococcus lanceolatus* (diplococcus pneumoniæ). Time will not permit me to give a full description of these here.

When after an operation the patient has died without having exhibited the characteristic symptoms of septicæmia, the death has not usually been attributed to septic infection, but rather has been supposed to be due to "heart failure," shock, pneumonia, suppression of the urine, or some other more or less satisfactory cause. But when the patient dies even less than twelve hours after an operation, we cannot positively exclude sepsis as the cause of death until the fact has been proven by an autopsy made by a competent pathologist and bacteriologist. I have witnessed autopsies where none of the local lesions which attend septic inflammation were demonstrable to the naked eye. Cover-slip examinations, however, showed the presence of organisms in large numbers, and tubes inoculated with the same fluid gave the characteristic growths. It is undoubtedly more comforting to the feelings of the operator to attribute the result to any cause other than septic infection, since he is naturally unwilling to think that his technique has been faulty. Those surgeons, however, who have had a bacteriological training, and are therefore best able to judge, are often the most ready to admit the possibility that infection of the wound has occurred through some slip during the operation. At the same time realizing, as they do, the manifold ways in which such accidents can occur, they are much more likely to avoid them.

By *asepsis* we understand that condition in which there is complete absence of septic material—a condition which of course can be ensured only by excluding all pathogenic micro-organisms from the site of operation.

We do not indeed always have a sterile wound, because it is probable that most fresh wounds contain a certain number of organisms. These, however, may either be non-virulent, or they may be present in too small numbers to give rise to the phenomena of sepsis.

The maintenance of an aseptic condition is certainly one of the most important points to be aimed at in formulating a technique of operative surgery. It is true that an ideal technique which will be aseptic from a bacteriological stand-

point has not yet been attained, and to protect our wounds so as not to allow the ingress of even a single bacterium is scarcely ever possible, at least at the present day; but those who control their technique by bacteriological experiments, and strive in every way to approach as nearly as possible such an ideal, constantly aiming at perfect cleanliness in their work, will undoubtedly obtain better results than those who have no such standard.

Bacteriology has shown us that while infection from the air is comparatively rare, it is most frequently brought about by contact. We can thus readily understand the comparative uselessness of the carbolic spray, and the uncertainty of antiseptic measures as applied to wounds, and can appreciate rather the importance of preventing the introduction of bacteria into the wound by means of the instruments or the hands of the operator and of his assistants.

By the term *antisepsis* we understand the various means used for destroying bacteria, or of so inhibiting them in their action as to render them incapable of giving rise to infection. The agents which are employed to bring about this condition are known as antiseptics and disinfectants, the latter name applying only to those agents which kill pathogenic or putrefactive organisms and which may consequently be termed true germicides, the former to the agents which arrest putrefaction or fermentation, but do not necessarily destroy the micro-organisms. The principles underlying disinfection and the general methods employed in practice will be found elsewhere; suffice it to say now that in operative surgery antiseptic measures or *disinfection* must be relegated to the time preceding the operation.

The association of laboratory with operative clinical experience must continue. We have learned much, but there is a promise of still greater progress to be reached in this way. While we deprecate the adoption of methods based solely upon laboratory experiments, experience having too often shown the inexpediency of such a procedure, we would insist most strongly upon the necessity of the harmonious working together of the surgeon and clinician with the bacteriologist, believing that each and all will in this way gain new facts and new points of view.

If, however, the surgeon has himself had preliminary instruction in bacteriology he will not only be able to temper the zeal of the workers in the laboratory by his clinical experience, but at the same time he will value at its true practical worth the suggestions which are the outgrowth of experimental work.

It must not be thought, however, that in our enthusiasm for asepsis and aseptic measures we would undervalue at all the importance of a perfected mechanical technique. Besides depending upon the presence or absence of the "seed"—the bacteria—the question of infection or immunity is influenced to a great extent (as we have also found by our laboratory experiments) by the condition of the "soil"—the tissues and fluids of the individual. Our more modern knowledge of wounds and wound infection, far from making us undervalue the skill of the surgeon, makes clear to us the necessity for operative precision. Linear incisions, the avoidance of any rough handling of the tissues and of the use of irritating fluids in the wound, the filling of dead spaces with substances having their origin in the body (serum, moist blood-clot, known to have definite germicidal power), the abbreviation of the time required for operations, the maintenance of hygienic surroundings, and the adoption of every means for strengthening the vital resistance of our patients, all will contribute largely to a surgeon's success.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of October 23, 1893 (continued).

DR. KELLY in the Chair.

A Case of Gas-Poisoning.—DR. HEWETSON.

J. C., male, aged 47, was admitted to Dr. Osler's wards on the 25th of September. He was first seen in the outdoor department at 2.30 p. m., having been brought to the hospital in the patrol-wagon by some men who said that he had been overcome by gas while working over street pipes at about 11 o'clock that morning. They also said that patient had suffered from several similar attacks, due to gas-poisoning, and that he had always recovered a short time after being pulled out into the fresh air, but that on this occasion, although he had been under a physician's care ever since the accident, he had shown no signs of returning consciousness. A fuller history was obtained from a foreman who was seen at 7 p. m. the same day. It was briefly as follows: He and patient were working together in a ditch upon the city gas pipes. A pipe had been removed, as I understand it, and the ends thus left open had been plugged with rubber stoppers used for that purpose. The foreman had cautioned patient to be very careful, as he had had several previous attacks, and left him for about three minutes, at the end of which time he returned to find him lying insensible in the trench.

When seen in the dispensary the patient was unconscious, with respirations 40 to the minute, not shallow; expiration prolonged, wheezing, and accompanied by groan. The face was cyanosed; lips blue, veins prominent. The eyes were rolled constantly from side to side; pupils equal, somewhat dilated; reacted to light. The corneal reflex was still present. Pulse 140, full and of high tension.

The muscles generally presented a marked tetanic condition, the head being held rigidly, and the jaw firmly fixed, although the teeth were from time to time ground together; the arms, rigidly held in a partially flexed condition, rested upon the thorax; the legs were fully extended and stiff. Slight clonic spasms occurred from time to time in both legs and arms. The patient was given $\frac{1}{100}$ grain of nitroglycerine and removed to the ward.

When seen at 3 p. m., temperature was 100°, respirations 42. The chief difficulty seemed to be in expiration, which was prolonged and noisy. The color of face was rather pale and the veins were much less prominent. The pulse, still about 140, was very much lower in tension. The muscles presented the same tetanic condition, arms and legs could be flexed only with difficulty; the deep reflexes were much exaggerated, a marked patellar and ankle clonus being present, while a sharp tap upon the quadriceps tendon produced a clonus in the entire leg. The chest was clear on percussion; coarse, moist râles were heard everywhere on auscultation, especially accompanying expiration, which was prolonged.

The heart dulness was not increased. Apex-beat not visible. Auscultation unsatisfactory, owing to noisy respiration. The abdomen was negative on examination, no bright red spots were noted here or elsewhere; there had been, however, involuntary passage of both urine and fæces.

Blood at 4 p. m. showed no changes beyond a moderate reduction of the hæmoglobin. Red corpuscles 5,216,000, in a cmm., white corpuscles 9,500. Hæmoglobin 73 per cent. Fresh specimens showed no poikilocytosis; centres of red cells showed no especial pallor.

On the 26th, patient presented much the same condition, universal rigidity of muscles persisting. Pupils moderately dilated, 4–5 mm. in diameter, were equal and reacted to light. Temperature at 8 p. m. rose to 101°. Nutritive enemata were ordered, as patient was not able to swallow.

On the morning of the 27th, at 7.15 and 7.30 respectively, the patient had two convulsive seizures, each lasting a few minutes. There was general clonic spasm of the muscles; the mouth was open, the tongue was protruded, and the jaw moved to the right; the arms were flexed, the hands clenched and held rigidly on chest; pulse 86, respiration 26. After these patient returned to his former condition, which has already been described, the coma persisting, the urine and fæces being still passed involuntarily. Enough of the former was obtained for examination, and was found to be yellow amber in color, clear, acid, s. g. 1023. A faint trace of albumen was present, but no sugar and no diazo-reaction. The microscopical examination was negative. During the afternoon two other convulsive attacks occurred, and two more during the night. Temperature rose to 101.8°.

September 28.—Patient still unconscious, presents almost same appearances as yesterday; conjunctival reflex is, however, present, and the muscular rigidity is less marked; ankle and patellar clonus absent, though the knee-kicks are still active. Temperature at 8 a. m. was 103°; respiration 38, coarse expiratory wheezing; pulse 96, regular in volume and rhythm, but of rather low tension. Chest everywhere clear on percussion: in- and expiration accompanied by loud snoring and sibilant râles.

A spectroscopical examination was made of the blood and its spectrum compared with that of normal blood both before and after the addition of a reducing agent, but no distinct difference could be detected.

September 29.—Still profoundly unconscious, respirations 30–32; pulse 96, of good volume; temperature has since yesterday ranged from 102°–103°. Rigidity much less in arms, still present in legs. Still passes urine and fæces involuntarily; the former shows nothing abnormal beyond a trace of albumen.

September 30.—During the afternoon of the 29th patient had several convulsive seizures. Face drawn and pinched, pale; eyes closed, eyeballs rolled up, pupils equal and somewhat dilated; react to light. Pulse 108, tension low. Respirations 48, expiratory groan and gurgle. Two small, bright red spots are seen over left eyebrow for the first time this morning. These disappear on pressure, to return instantly. The arms are to-day rigidly extended, can only be bent with difficulty, and immediately straighten out again with considerable tremor. On the other hand the legs are not nearly so rigid and can be bent easily, especially the right. Knee kicks still present, most marked on the left side. Temperature still high.

Note at 4 p. m.—Since midday the patient has become much worse; respiration noisy, 60 to the minute; pulse 120–130, feeble. There is now for the first time deficient resonance over the right scapular region, but no altered quality in the breath-sounds can be made out, possibly owing to the noisy, bubbling râles everywhere present. No extension of cardiac dulness to the right can be made out. A small amount of urine obtained was hazy, ammoniacal, but showed a distinct trace of albumen and many granular casts. The patient has swallowed some stimulant during the past 24 hours in addition to that given in the nutritive enemata, which have not been well retained. Strychnia $\frac{1}{30}$ grain ordered for two doses.

Note of October 1st.—No signs of consciousness, face pale, bathed in perspiration. Respiration noisy, 60; slight discharge of a yellow frothy fluid from the mouth. Pulse 99, small and feeble. Arms rigidly extended, as are also the legs. The left leg can, however, be bent with but little difficulty, presenting in this respect rather a striking contrast to the right, which is flexed with great difficulty and gives a marked patellar and ankle clonus. The knee-kick alone is slightly increased on the left side. The same dulness persists in right scapular region. Ether thirty minims every two hours was ordered hypodermically. The patient grew, however, gradually worse during the day, respiration became more labored, gurgling, and was accompanied by the discharge of a yellow frothy fluid from the nose and mouth. The pulse grew gradually weaker and death occurred at 7.35 p. m., the temperature having ranged during the day from 102°–104.8°.

While cases of carbon monoxide poisoning are not rare in Baltimore, it even being mentioned by Kobert[1] as a city in which from 6 to 14 deaths occur yearly from this cause, nevertheless, as this is the first case we have had in this hospital, and as there is a dearth in the literature of reports of clinical observations extending over a comparatively long time, coupled with a thorough autopsy, we have thought it worth while to report the case somewhat fully.

Probably the reason that Baltimore is so unfortunate in this respect is the fact that we use here, as I am told, the "water-gas," which may contain as much as 30 per cent. of carbon monoxide, or five times as much as is usually found in ordinary illuminating coal gas. The former, too, differs from the latter in having comparatively little or no smell, so that the danger of poisoning from it is much increased.

In making a diagnosis in a probable case of gas-poisoning, one has first to consider the history; and in this case it is almost conclusive. Still, even in its absence, the appearance of the man when first seen, and the symptoms which subsequently developed, correspond in every way to the description given by Caspar,[2] Becker,[3] Kobert[4] and others, of cases of carbon monoxide poisoning. The first examination of the urine was useful in exclusion, as with a normal specific gravity the fact that only a faint trace of albumen was present relieved the kidneys of responsibility in the matter, and inasmuch as, according to Kobert, albuminuria exists in at least 20 per cent. of all cases of carbon monoxide poisoning, the presence of this small amount in the patient's urine on entrance is not at all surprising. That the urine three days later showed a distinct ring of albumen and many tube casts was strongly suggestive of some severe intoxication. The presence of sugar or some reducing substance in the urine, *e. g.* glycuronic acid, has been demonstrated by Litten[5] in 70 per cent. of all his cases. The test was made in our case only with Fehling's solution, and possibly a very small quantity may have escaped detection.

Until comparatively lately it was believed that death and the symptoms which precede it in carbon monoxide poisoning were due almost entirely to the so-called "paralysis of the red blood cells," *i. e.*, to the combination of CO with the hæmoglobin of the red cells, which prevents them from acting as oxygen-carriers. Although carbon monoxide forms a loose chemical compound with the hæmoglobin, yet it has an affinity for it some 200 times greater than has oxygen, and it is therefore easy to understand its poisonous nature, since while carbon monoxide gas readily displaces oxygen, the latter does not readily, and indeed can only slowly displace CO from its combination with hæmoglobin.

But while every one recognizes the importance of this change in the blood, yet the direct action of the CO upon the tissues of the body can now no longer be denied. As an example of this, Kobert refers to the fact that "explosive-like" symptoms, cramps

[1] Lehrbuch der Intoxicationen, 1893, S. 524.
[2] Handbuch d. gerichtlichen Medicin.
[3] Vierteljahrschrift f. gerichtliche Medicin, 1893, Heft 1 und 2.
Loc. cit.
[4] Cit. by Kobert.

and paralyses of the extremities, may follow, even within the first minute, the inhalation of air containing not less than 20 per cent of carbon monoxide, long before these could be accounted for by the saturation of the blood with the gas. He goes even further and claims, on the ground of experiments as yet unpublished, that not only are the ganglion-cells of the nerve centres affected, and the peripheral nerves and muscles, but degenerations develop more quickly in them, and extend too far for it to be possible to explain them as simple asphyctic phenomena.

Geppert[1] maintains that carbon monoxide has a primary specific harmful influence on the nerve centres, since, while in ordinary asphyxia the withdrawal of oxygen can be made up for by the increase in the number and depth of the respirations, in carbon monoxide poisoning, with similar oxygen limitation, animals are wholly unable to reinforce their respiratory capacity. Again, the fact upon which all authors agree, viz., that the rigidity, spasms and convulsions may persist for some time after the CO has disappeared from the blood, and that in some cases paralyses may follow, points strongly to the implication of the nerve centres.

Becker[2] reports a severe case of poisoning where coma lasted for quite a long time, the patient being unable to swallow until the fourth day, and unable to recognize his wife until the eleventh day. The convulsions were severe and lasted for eight days. The patient recovered, but multiple disseminated sclerosis followed.

The action of the poison on the vasomotor centres is shown by the high-tension pulse and violent action of the heart, due to their stimulation, and later by the rapid pulse of low tension, due to their paralysis. Kobert explains the occurrence of the bright red spots as being due to a circumscribed paralysis of the vasomotor nerves over small areas in the skin. The respiratory centres he believes to be affected in the same way, but in them the primary stimulation may last longer.

Blood.—The spectroscopical examination of the blood, while satisfactory for the diagnosis in cases in which large amounts of carbon monoxide are present, cannot be relied upon when less than 27 per cent of the hæmoglobin is saturated with the gas. The technique of the examination is not complicated, but requires some little practice in the use of the spectroscope. The spectrum of CO-hæmoglobin resembles very closely that of oxyhæmoglobin, as well as that of hæmochromogen, when the solutions used are of the same concentration, and the layers of fluid examined are of the same thickness. All three substances give two absorption bands between D and E. The bands of the CO-hæmoglobin are situated a little further to the right, *i. e.* towards the violet end, than are those of oxyhæmoglobin, while those of the hæmochromogen are still further to the right, so that they may go even beyond the line E. Although one can, by placing the two spectra the one over the other, distinguish the CO-hæmoglobin from the oxyhæmoglobin, there is a much simpler method of proceeding. If one adds a reducing substance, such as ammonium sulphide, to the normal blood, its spectrum no longer has two absorption bands between D and E; in other words, the spectrum of reduced hæmoglobin is obtained; whereas if 27 per cent or more of the hæmoglobin be combined with CO, the spectrum, on the addition of the ammonium sulphide, still retains its two bands unaltered. This affords a ready means for distinguishing the spectra, but it must not be forgotten that the test holds good only when more than one-fourth of the hæmoglobin in the blood is combined with CO.

The color of blood which contains a large amount of CO in combination, varies from a violet to a bright cherry red, and the violet froth which appears on shaking distinguishes it in a striking way from normal blood. In case a spectroscopical examination of the blood is for any reason not practicable, the chemical examination will always determine the presence or absence of CO. The palladium chloride test as modified by Fodor, and the ammonium sulphide and acetic acid test of Salkowski and Katagama, are probably the best.

Becker[1] asserts that under two conditions it is impossible to prove the presence of CO in the blood spectroscopically: (1). "If the patient has been brought out of the poisonous atmosphere into the fresh air and has breathed there for some time before death." (2). "If the source from which the poisonous gas escapes has been shut off before death occurred, so that during the last respirations fresh air has been inhaled, the carbon monoxide disappears from the blood after some time."

Caspar[2] makes the following statement: "If in a case of doubtful poisoning, in which circumstances point to carbon monoxide as being the cause, and in which the post-mortem examination shows nothing to oppose this view, but in which the addition of ammonium sulphide to the blood causes a reduction of the hæmoglobin, one must state that, although the result does not prove such a poisoning, it does not exclude it, but rather that such a poisoning is possible, and even probable. One may declare oneself much more positively from a general consideration of the whole case."

From what has been said it is not surprising that we failed to detect the presence of carbon monoxide in the blood in this case, as the spectroscopical examination was not made until the third day after entrance, and after a careful consideration of all the various points, viz., the history, the marked cyanosis, dyspnœa, the involuntary passage of urine and fæces, the condition of the pulse, the presence of the small, bright red spots on the skin, the prolonged coma, the peculiar varying rigidity of the muscles with exaggerated reflexes, the terminal broncho-pneumonia and marked œdema of the lungs, I think we are justified in making a positive diagnosis of carbon monoxide poisoning, more especially as there was nothing in the post-mortem examination to oppose such a view.

Opinions differ very much regarding the treatment of such cases. All authors agree in advising artificial respiration; many recommend in addition to this the inhalation of oxygen gas. Others with Hoffmann,[3] Kloman,[4] Dooley[5] and Crossland,[6] claim to have obtained good results from the use of nitroglycerine. Many believe in bleeding, others in transfusion of blood or normal salt solution. Dr. Halsted, in an article published in the "Annals of Anatomy and Surgery," 1884, strongly recommends the refusion of defibrinated blood, and reports two cases where, after withdrawing several hundred cubic centimetres of the patient's blood, he defibrinated and returned it centripetally into the radial artery with good results. This treatment seems most rational if carried out soon after the poisoning has occurred, but if, as Becker claims, the CO is very speedily eliminated from the blood, and the serious after-symptoms are due to the effects which have been produced by it upon the tissues generally, and more particularly those of the nervous system, as would seem to be the case, the procedure is probably not so useful in the later stages. Indeed, until the true nature of the lesions in the central nervous system is better understood we shall have to fall back upon symptomatic treatment.

Notes of Autopsy by Dr. Flexner.—Autopsy at 10 a. m., 14 hours after death. The anatomical diagnosis is as follows: Œdema of cerebral meninges; aspiration pneumonia; acute fibrinous pleurisy; chronic diffuse nephritis; congestion of colon and stomach; chronic peri-hepatitis.

The external appearances in this case were in no way remarkable, with the possible exception of a number of bluish-red spots over a

[1] Geppert: Deutsch. med. Wochenschr. 1892, No. 19, p. 418.
[2] Deutsch. med. Wochenschr. 1889.

[1] Vierteljahrschrift f. gerichtliche Medicin, 1893, Hefte 1 und 3.
[2] Handbuch d. gerichtlichen Medicin, S. 602.
[3] Allgemeine medicinische Central Zeitung, Berlin, No. 13.
[4] Maryland Medical Journal, 1890.
[5] New York Medical Journal, 1890.
[6] *Ibid.* 1890.

bald spot on the occiput. There was, however, beginning post-mortem discoloration of the abdominal walls; the finger-nails were cyanosed. The pupils were of middle width and equal in size; rigor mortis was present.

The cerebral lepto-meninges were œdematous; the veins in the meninges, both brain and cord, were distended with blood. The weight of the brain after dissection was 1480 grams. There were no gross lesions to be made out either in the brain or the cord.

The mucous membrane of the pharnyx, larnyx and trachea was somewhat congested. In the latter there was a small quantity of viscid mucus.

Both lungs were voluminous and did not retract on the removal of the sternum. The pleura on both sides was free from old adhesions. In the upper lobes of both lungs were discrete foci of broncho-pneumonia. These were more numerous in the right than in the left upper lobe. They were dark grayish-red in color, elevated above the cut surface of the lung, slightly granular in appearance, and on pressure thick muco-pus could be squeezed from the corresponding bronchi. From the lung tissue generally much blood-stained serum was obtained on squeezing the surface. The lower lobes, especially the right lower lobe, also contained broncho-pneumonic areas. Over the pleura where these consolidated foci came to the surface, a fine granular deposit was present.

The pericardial cavity contained a small quantity of clear serum. The heart weighed 300 grams; its valves were normal. The right ventricle was distendedwith dark fluid blood and fresh dark clots. The heart's flesh was easily torn.

The liver weighed 1900 grams. The capsule, especially over the right lobe, was thickened. The consistence of the liver was diminished, its sharp edges rounded, and the lobules were quite distinctly visible.

The spleen weighed 130 grams. It was somewhat softened. The lymphatic apparatus could be made out distinctly.

The kidneys together weighed 280 grams. The capsule, which was somewhat adherent, on removal left the surface roughened, and disclosed a few small cysts filled with clear contents. The cortical substance was somewhat opaque, and yellowish in color. The pelves and ureters apparently were normal. The bladder contained 300 ccm. of slightly turbid urine. There was nothing abnormal to be seen in this organ, neither in the adrenal glands, thyroid gland and pancreas.

With the exception of the mucous membrane of the colon, which was congested, the intestine appeared normal. The mucous membrane of the stomach also showed a few congested patches.

Frozen sections of the kidney showed a moderate increase of the connective tissue, not generally distributed, but occurring in foci. The epithelium of the convoluted tubules contained fat droplets; generally it was granular and swollen. The heart muscle was not fatty, but contained an increased amount of muscle pigment.

Bacterioscopic.—The cerebral menengis did not show any organisms in the cover-slips, nor were any obtained in cultures. Cover-slips from the lungs showed, besides many typical pneumococci occurring in pairs and short chains, a moderately large number of bacilli growing singly and in short chains. Both of these forms were sometimes free, sometimes enclosed in cells. Other organs were sterile.

The cocci in the lung grew on suitable culture media in the manner characteristic of the diplococcus pneumoniæ. The bacillus was not identified. In morphology it resembled the bacillus coli communis, but in gelatine it did not grow characteristically, and it has likewise failed to coagulate or produce any noticeable change in milk after one week in the thermostat at 37.5° C.

Tissues from the brain and spinal cord were transferred immediately to various fixing and hardening agents, including absolute alcohol, Flemming's solution, and Müller's fluid. Owing to an accident, those from the brain were lost, so that the microscopical examination was limited to the cord. Sections prepared from various segments in the cervical, dorsal and lumbar regions and stained appropriately, depending on the fixing method employed, were studied. The sections of the cord fixed in Flemming's solution were stained in safranine, those hardened in Müller's fluid in hæmatoxylin and eosine and borax-carmine, as well as according to the method of Weigert for staining the myeline sheath, and of Marchi. No lesions were discovered either in the ganglion cells or in the nerves. The nuclei of the ganglion cells were perfectly preserved, vacuolation of the protoplasm of the cells was not observed, and other forms of degeneration were not found. The sections fixed in osmic acid (Flemming) showed a considerable quantity of dark granules in the cell protoplasm often covering and obscuring the nucleus. Dark pigment was observed, however, in other preparations, but it was perhaps not so dark and in smaller quantity.

In conclusion, this report must be regarded as entirely negative, so far as its bearing on the supposed carbon monoxide poisoning is concerned. We did not find any of the distinctive lesions of this condition. Peculiar alterations in the color and coagulability of the blood were not observed in this case, nor could the lesions described by Cramer, consisting of an extensive disappearance of nerve fibres, associated with a diffuse new growth of glia, be found, so far as our examination extended. The vacuolization of the ganglion cells which he observed in the cortex is not present in our case in the cord. However, in his case the affected individual lived much longer and was far advanced in age, so that the cases are perhaps not comparable. We likewise did not find the foci of softening described by Simon, nor the capillary apoplectic hemorrhages and meningeal ecchymoses mentioned by other writers. The clinical evidence is, however, so convincing that there can be but little doubt as to the nature of the intoxication.

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